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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
CUNNINGHAM, T	
ART UNIT	**PAPER NUMBER**
1816	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/474,388	Applicant(s) Springer et al.
	Examiner Thomas Cunningham	Group Art Unit 1816

☒ Responsive to communication(s) filed on *Oct 15, 1997* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *71-83 and 87-98* is/are pending in the application.

Of the above, claim(s) *87-98* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *71-83* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. Claims 71-83 are subject to examination. The amendment dated 10/15/97 is considered below. Upon reconsideration, the prior restriction requirement is reimposed for the reasons previously set forth. Additionally, due to the different laboratories involved in investigation of properties of ICAM-1-like molecules, too much search burden would be imposed in examination of distinct methods of use or preparation of ICAM-1 molecules.

2. Newly submitted claims 87-98 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: New claims 87-98 are directed to methods of making and using ICAM-1 polypeptides. The originally examined invention is directed to ICAM-1 polypeptides which may be alternatively used in diagnostic, therapeutic or research procedures. Additionally, such polypeptides may be made by different procedures, such as by chemical synthesis, recombinant DNA expression or by extraction from natural sources. Examination of the additional invention imposes an undue burden upon the Examiner in that issues pertaining to the now-claimed uses or now-claimed methods of making would have to be examined in addition to the ICAM-1 products themselves.

Since applicant has received an action on the merits for the originally presented (and provisionally elected) invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 87-98 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. (Maintained in part) Claims 71-83 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. (Withdrawn) The term "ICAM-1" when read in light of the specification has been interpreted as being limited to full-length, transmembrane human intercellular adhesion molecule 1, e.g. residues 1-505 as described in Fig. 8.

--The Examiner agrees with the interpretation set forth by the Applicant on page 6 of the last response.

B. (Withdrawn) In claims 71 and 80 it is unclear what the scope of the term "natural contaminants" is. Is this limited to cellular components found in human cells which express ICAM-1.

Does this term encompass contaminants from prokaryotic or eukaryotic cells which have been engineered to express ICAM-1?

--The Examiner agrees with the interpretation set forth by the Applicant on page 7 of the last response.

C. (Withdrawn) In claims 73 and 81 it is unclear what the scope of the term "bind lymphocytes" of "lymphocyte binding" is. Is this term limited to known ICAM-1 specific ligands like LFA-1 or does it generally encompass molecules such as lipids in the cell membrane to which the transmembrane domain of the molecule of ICAM-1 associates? Does it exclude binding to molecules like T cell receptors or T cell receptor accessory molecules like CD4 and CD8?

--This issue is withdrawn in view of the Applicant's comments on pages 7-8 of the response and in view of the amendment to limit to "specific" binding.

D. (Withdrawn) Claims 71, 80, 81, and 84-86 it is unclear what the scope of the terms "biological activity" or "biologically active" are. Are these terms limited to the ability of ICAM-1 to bind to HRV or LFA-1? Do they encompass immunological or

antigenic activity, e.g. the ability to induce or be bound by an antibody?

--This term has been interpreted in view of Applicant's comments on page 8 of the response. It is not limited to the ability of ICAM-1 to bind to LFA-1.

E. In claims 79 and 83 the term "has" has been interpreted as being open claim language comparable to "comprises".

F. (Maintained) In claims 75-78 the term "about" is vague and indefinite. (1) Is this term limited to 1%, 5%, 10%, 100% or less variation in the recited molecular masses? Where is it defined in the specification? (2) Is this intended to encompass a family of native ICAM-1 molecules with slightly different molecular masses as purified, e.g. by virtue of different degrees of glycosylation or expression of alternatively processed mRNA transcripts?

--Applicant's comments on pages 8-9 of the response have been considered, but do not adequately indicate the scope of this term.

G. (Withdrawn) In claims 71-79 it is unclear what the term "preparation" encompasses or excludes. Does this term require that the ICAM-1 product be produced by a particular preparative method or from a particular source, e.g. from natural sources such as cell lines like human spleen cells or JY cells? Is this term limited to ICAM-1 alone or does it include compositions comprising ICAM-1 and an excipient or carrier (e.g. a composition)?

--This term refers to any composition containing purified or isolated ICAM-1, see page 9 of the last response.

H. (Withdrawn) In claims 80-83 it is unclear what the scope of the term "lipid membrane" is. Is this limited to lipid bilayers formed of naturally-occurring phospholipids, sphingolipids or cholesterols? Does this term embrace ICAM-1 in detergent solutions or micelles? Does his term embrace liposomes?

--This term has been interpreted in accordance with the definition set forth by the Applicant on page 9 of the last response.

4. Claims 71-83 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the

specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A. The specification only describes ICAM-1 having the sequence set forth by Fig. 8. No other amino acid sequences for native ICAM-1 products with different sequences are described.

--Applicant indicates on page 10 of the response that ICAM with different molecular masses can be obtained using the methods described in the specification, e.g. by immunoprecipitation from different sources. However, the specification does not describe the critical structural characteristics of such other species of ICAM-1 and therefore represents an invitation to obtain other structurally-distinct forms of ICAM-1 of Fig. 8. Whether such other forms of ICAM-1 would have identical functional properties to the ICAM-1 of Fig. 8 or retain critical structural properties, e.g. ability to bind HRV or LFA-1 would be unpredictable. Further, it is unclear how much structure would have to be retained between an ICAM-1 variant and the ICAM-1 of Fig. 8 in order for it to be considered ICAM-1.

It is suggested that a family of structurally and functionally closely-related ICAM-1 variants may be adequately

enabled by reference to their cross-reactivity with particular monoclonal antibodies or their ability to bind to a member of the LFA-1 family of molecules. Applicant is encouraged to discuss an appropriate genus of ICAM-1 molecules with the Examiner in conjunction with a review of the priority documents, e.g. pages 16-21 of priority application 07/045,963.

B. The specification does not adequately describe which preparations of ICAM-1 retain particular biological properties such as the ability to bind to LFA-1, lymphocytes or HRV.

--Applicant's argument on page 11 is persuasive with respect to the ICAM-1 of Fig. 8, but not with respect to other ICAM-1 variants which have not been structurally and functionally described.

C. The specification only describes particular molecules on the surfaces of lymphocytes, such as LFA-1 or members of the LFA-1 family (CD11/CD18), which bind to ICAM-1.

--Applicant's comments have been considered, but in view of the broad intended definition of "biological activity" set forth in the Applicant's response to the rejection under 112/2 this rejection is maintained. This rejection would be withdrawn if

the biological activity were limited to those activities described in the specification.

D. (Maintained) The rejection set forth in section 6D of the last action is maintained in view of the broad scope of the term "biological activity". This rejection would be withdrawn if the claim language were limited to products with a demonstrated structure function relationship with a recited biological activity, such as the ability of residues in domains 1 and 2 to bind to LFA-1 or HRV.

5. Claims 71-79 and 86 are rejected under 35 U.S.C. 102(a) or (b) over Dustin et al., J. Immunology 137:245 (July 1, 1986). These claims are directed to ICAM-1 preparations from JY cells, human spleenocytes or myelomoncytic cells. Page 66 of the specification refers to Dustin et al. The abstract of this publication indicates that ICAM-1 displays Mr heterogeneity depending on the cell type from which it is isolated. The nonglycosylated form of ICAM-1 is taught to have an Mr of 55,000 Da.

The claims recited above all embrace forms of ICAM-1 that are identical to those taught by Dustin et al. I.e. the claims

encompass ICAM-1 recombinantly-produced in cell lines which would provide the same type of glycosylation as the native cell lines taught by Dustin et al.

--This rejection may be withdrawn if a signed copy of the 1.132 declaration is made of record in this application. -1.

6. (Maintained) Claims 71-79 are rejected under 35 U.S.C. 102(e) as being anticipated by Greve, U.S. patent 5,589,453 (priority to 9/1/88). The cited patent, columns 4-7, teaches human rhinovirus receptor protein (now referred to as ICAM-1) prepared from HeLa cells with an Mr of about 95,000 Da and tryptic fragments of ICAM-1. Claims 71-74 are anticipated because the prior art HRRP (ICAM-1) would inherently have the biological activities of native ICAM-1, such as antigenicity, ability to bind LFA-1, lymphocytes or HRV. Greve specifically teaches that ICAM-1 binds to HRV, see e.g. claims. The molecular mass limitations of claims 75-78 are anticipated by the HRRP (ICAM-1) of Greve et al because the 95,000 Da ICAM-1 protein of Greve has been interpreted as being "about" 72-91 kDa, 76.5-97 kDa, 114 kDa and 97 kDa thus meeting the limitations of claims 75-78. HRRP of Greve (ICAM-1) would inherently have the amino acid sequence of Figure 8, thus meeting the limitation of claim

79. The eukaryotically-expressed ICAM-1 of claims 84 and 86 embraces the 95,000 Da HRRP (ICAM-1) of Greve.

The lipid membranes comprising isolated of purified ICAM-1 of claims 80-83 are anticipated by the detergent-isolated ICAM-1 of Greve. Detergent isolated ICAM-1 would be conmplexed with hydrophobic detergent moieties in membranous micellar forms and would inherently retain the functional binding activities of the native molecule as evidenced by Greve's disclosure that it binds HRV.

--Applicant's arguments on page 13 of the last response have been considered. It is acknowledged that Applicant's do not necessarily agree that Greve is entitled to a 102(e) date of September 1, 1988. Applicant urges that the instant application (and invention?) is entitled to a priority date of May 4, 1987 tracing priority back to 07/045,963.

Application 07/045,963 has been reviewed and describes and claims ICAM-1 and functional derivatives of ICAM-1 free of natural contaminants. It does NOT describe biological activities such as the now known ability of ICAM-1 to bind to human rhinoviruses. It does describe the ability of ICAM-1 to bind to LFA-1. However, there appears no basis for priority for product claims limited to "at least one biological activity of native

ICAM-1" where that activity may be interpreted to embrace HRV-binding fragments of ICAM.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas M. Cunningham, Ph.D, J.D. whose telephone number is (703) 308-3968.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

THOMAS M. CUNNINGHAM
PRIMARY EXAMINER
GROUP 1800